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Application Serial No.: 09/287,573

Express Mail No. EV 298 967 374 US

Filing Date: April 6, 1999

PATENT

Attorney Docket No. A-67207-2/RMS/DCF/NHT (469420-26)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

WALT *et al.*

Serial No.: 09/287,573

Filed: April 6, 1999

For: *Self-Encoding Sensor with
Microspheres*

Group No. 1641

Examiner: Gabel, Gailene

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

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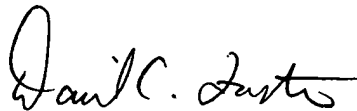
Sir:

Enclosed for filing are the following documents:

- 1) Response to Restriction Requirement;
- 2) Express Mail No. EV 298 967 374 US Certificate; and
- 3) Return postcard.

Respectfully submitted,

DORSEY & WHITNEY LLP



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Robin M. Silva, Reg. No. 38,304
Filed under 37 C.F.R. § 1.34(a)

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Dated: 26 January 2004

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RESPONSE TO RESTRICTION REQUIREMENT

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This paper is submitted in response to the Restriction Requirement mailed December 30, 2003. This response is timely filed on or before January 30, 2004. Although Applicants do not believe any additional fees are required, the Commissioner is authorized to charge any additional fees, including extension fees or other relief which may be required, or credit any overpayment to Deposit Account No. 50-2319 (Order No. A-67207-2/RMS/DCF/NHT (469420-26')).

Claims are reflected in the listing of claims, which begins on page 2 of this paper.

Remarks begin on page 7 of this paper.

Listing of Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-15 (previously canceled)

16. (previously amended) A method for increasing the signal-to-noise ratio in the characteristic optical response of an array having subpopulations of sensor elements comprising:

- a) providing an array comprising:
 - i) at least a first subpopulation comprising first sensor elements; and
 - ii) a second subpopulation comprising second sensor elements;
- b) contacting said array with a composition comprising at least a first target analyte;
- c) obtaining a first measurement from at least two of said sensor elements of at least one of said subpopulations;
- d) summing said first measurements from said sensor elements; and
- e) performing a statistical analysis on said first measurements.

17. (previously amended) The method according to claim 16 further comprising obtaining at least a first control measurement and adjusting the baseline of said first measurement against said first control measurement.

18. (previously amended) The method according to claim 16 wherein the signal-to-noise ratio is increased by a factor of at least 10.

19. (original) The method of claim 16 wherein an analyte detection limit is reduced by a factor of at least 100.

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20. **(currently amended)** The method of claim 16[[, 25]] or 27, wherein said sensor elements are beads and said array comprises a population of beads dispersed on a substrate.
21. **(original)** The method of claim 20 wherein said substrate is a fiber optic bundle.
22. **(original)** The method of claim 20 further comprising identifying the location of each sensor element within each sensor subpopulation within the array.
23. **(original)** The method according to claim 16 wherein said sensor elements comprise chemical functional groups.
24. **(original)** The method according to claim 16 wherein said sensor elements comprise oligonucleotides.
25. **(canceled)** A method for amplifying the characteristic optical response of an array having subpopulations of sensor elements comprising:
- a) providing an array comprising:
 - i) at least a first subpopulation comprising first sensor elements; and
 - ii) a second subpopulation comprising second sensor elements;
 - b) contacting said array with a composition comprising at least a first target analyte;
 - c) obtaining a first measurement from at least two of said sensor elements of at least one of said subpopulations; and
 - d) summing the optical responses.
26. **(canceled)** A method according to claim 25 further comprising obtaining at least a first control measurement and adjusting the baseline of said first measurement using said first control measurement.

27. **(previously amended)** A method comprising:
- a) providing an array with a plurality of subpopulations of sensor elements;
 - b) contacting said array with a composition comprising at least a first target analyte;
 - c) obtaining first and second measurements from at least first and second sensor elements, respectively, from at least a first subpopulation; and
 - d) performing a statistical analysis on said first and second measurements.
28. **(currently amended)** The method according to claim 16[[, 25]] or 27, wherein each subpopulation comprises a bioactive agent.
29. **(original)** The method according to claim 28, wherein at least one of said bioactive agents is a nucleic acid.
30. **(original)** The method according to claim 28, wherein at least one of said bioactive agents is a protein.
31. **(previously amended)** The method according to claim 20, further comprising determining outlying beads and excluding outlying beads from said subpopulation.
32. **(previously amended)** The method according to claim 16, 45 or 27, wherein said statistical analysis comprises calculating the mean of at least said first and second measurements.
33. **(previously amended)** The method according to claim 16, 45 or 27, wherein said statistical analysis comprises calculating the standard deviation of at least said first and second measurements.

34. **(currently amended)** The method according to claim 16[[, 45]] or 27, further comprising evaluating the statistical validity of said measurements.
35. **(previously amended)** The method according to claim 16[[, 45]] or 27, further comprising performing a second statistical analysis on said measurements.
36. **(original)** The method according to claim 35 wherein said second statistical analysis comprises evaluating said measurements using confidence intervals.
37. **(original)** The method according claim 35, wherein said second statistical analysis comprises using said measurements to perform hypothesis testing.
38. **(currently amended)** The method according to claim 16[[, 45]] or 27, further comprising comparing said statistical analysis of measurements obtained from at least two subpopulations.
39. **(original)** The method according to claim 38, wherein said statistical analysis comprises performing a cluster analysis of said subpopulation.
40. **(previously amended)** A method comprising:
- a) providing an array comprising beads on a substrate comprising a plurality of subpopulations of sensor elements, wherein each sensor element comprises a bioactive agent that will bind a target analyte, and at least two of said subpopulations comprise different bioactive agents that will bind the same target analyte;
 - b) contacting said array with a composition comprising at least a first target analyte;
 - c) obtaining a measurement from the optical response of each sensor element; and

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- d) performing a statistical analysis on said measurements from each sensor element.

41. **(original)** The method according to claim 40, wherein at least two of said subpopulations each comprise bioactive agents that will bind different target analytes.

42. **(original)** The method according to claim 41, wherein at least one of said bioactive agents is a nucleic acid.

43. **(original)** The method according to claim 41, wherein at least one of said bioactive agents is a protein.

44. **(original)** The method according to claim 40, further comprising, determining outlying beads and excluding outlying beads from said subpopulation.

45. **(canceled)** The method according to claim 25, further comprising:

- e) performing a statistical analysis on said measurements of at least one of said subpopulations.

46. **(currently added)** The method according to claim 16,[[25,]] 27 or 40, wherein said substrate is selected from the group consisting of glass and plastic.

47. **(previously added)** The method according to claim 20, wherein said substrate is selected from the group consisting of glass and plastic.

48. **(previously added)** The method according to claim 17 [[or 26]]wherein said adjusting comprises subtracting said first control measurement from said first measurement.

REMARKS

Claims 16-48 are pending in this application and are subject to a restriction requirement. Claims 25, 26, and 45 have been canceled, without prejudice or disclaimer, as drawn to a non-elected invention. Claims 20, 28, 34, 35, 38, 46, and 48 have been amended to remove dependency on canceled claims 25, 26, and 45. No new matter has been introduced by way of these amendments.

Response to Restriction

In response to the Restriction requirement, Applicants elect Group III, namely claims 20-22, 27-39, 46, and 47, for further prosecution on the merits. This election is made with traverse. Applicants request reconsideration of the restriction requirement in view of the following remarks.

Applicants submit Group III, drawn to a method that includes statistical analysis of measurements from an array of a plurality of sensor elements, is generic and Group I and IV are proper species of that genus. M.P.E.P. § 806.04(d) defines a generic claim to be one that comprehends within its confines the organization covered in each of the species. In particular, the generic claim cannot include limitations not present in each of the species. In the instant case, all the elements of independent claim 27 of Group III are found in Groups I and IV. All three groups have an array with a plurality of sensor element subpopulations. All three groups contain a step of contacting the array with a composition comprising at least a first target analyte. All three groups contain a step wherein measurements are obtained from at least two elements of at least one subpopulation of the sensor elements. Finally, all three groups claim a statistical analysis of those measurements. Thus, Group III properly reads on the claims of Groups I and IV and satisfies the requirements for a genus claim. The commonality of these elements within all three groups thereby prevents restriction between the inventive groups.

M.P.E.P. §809.02 and 37 CFR §1.146 provides that if an application contains a generic claim linking a number of species claims, a restriction requirement is limited to a proper

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election of species. The rationale is that if the species claims are written in dependent form or include all the limitations of the generic claim, the species claims are necessarily allowable if the generic claim is found allowable. Importantly, there is no serious burden on the Examiner because, should a generic claim be allowable, no further search is required as to the other related species claims. Hence, as provided in 37 CFR §1.141(a) and MPEP §809.03, the presence of a generic claim prevents restriction between inventions that are otherwise divisible. In these circumstances, a proper restriction is to an elected species, and requires the Examiner to (a) identify the generic claim, (b) clearly identify each of the disclosed species to which claims are to be restricted, and (c) require applicant to elect a single disclosed species. *See* MPEP §809.02(a).

Furthermore, as the Examiner is aware, M.P.E.P. § 803 states that, "[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions." Here, the inventive steps that distinguish Groups I and IV from Group III would not pose an undue search burden on the Examiner. For example, Group I claims an additional step of summing the first measurements from the sensor elements. Likewise, Group IV further defines the sensor element subpopulations to comprise different bioactive agents that will bind the same target analyte. Given the overlapping nature of the three groups, the one additional element with respect to each species claim would not constitute a serious search burden.

In view of all of the foregoing, Applicant requests that the restriction requirement be reformulated to a single inventive group encompassing the subject matter of Groups I, III, and IV be examined together, in accord with MPEP guidelines and statutory requirements.

Inventorship is not affected by cancellation of the non-elected claims.

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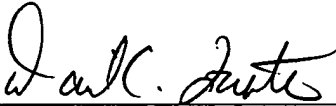
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CONCLUSION

Please direct further questions in connection with this Application to the undersigned at (415) 781-1989.

Respectfully submitted,
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Filed under 37 C.F.R. § 1.34(a)